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(21) International Application Number: PCT/GB00/00475 (22) International Filing Date: 11 February 2000 (11.02.00) (30) Priority Data: 9902976.1 11 February 1999 (11.02.99) GB (71) Applicant (for all designated States except US): GILTECH LIMITED [GB/GB]; 9/12 North Harbour Estate, Ayr KA8 8BN (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): HEALY, David, Michael [IE/GB]; Midton House, By Alloway, Ayr KA7 4EG (GB). GILCHRIST, Thomas [GB/GB]; The Lodge, 67 Midton Road, Ayr KA7 2TW (GB). (74) Agent: MURGITROYD & COMPANY; 373 Scotland Street, Glasgow G5 8QA (GB).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: BIODEGRADABLE COMPOSITE MATERIAL FOR TISSUE REPAIR (57) Abstract There is described a biodegradable composite material for tissue repair comprising a water-soluble glass, preferably as glass fibres and/or particles in the form of a matrix, impregnated with a biodegradable polymer. An especially preferred polymer is poly ϵ -caprolactone. The biodegradable composite is particularly useful for the repair of nerve and/or bone tissue, especially the bones of the skull. A method of producing the composite material is also described.		

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1 **Biodegradable Composite Material for Tissue Repair**

2

3 The present invention relates to a composite material
4 which is especially useful in bone repair.

5

6 Most commonly defects to bone arise from injury, but
7 may also be due to congenital abnormalities, to
8 acquired deformity or to ablation of tumours. Without
9 adequate repair, bone defects can significantly affect
10 function of the associated limb, and frequently the
11 mobility of the patient is impaired. Where the bone
12 defect is present in the skull, there may be cosmetic
13 considerations and without adequate repair the
14 appearance of the patient may be adversely affected.

15

16 Repair and reconstruction of defective bone currently
17 involves either the use of auto-graft tissue (ie where
18 bone is removed from another part of the patient's body
19 and used for repair) or the use of bio-compatible
20 materials. Allograft bone transplants (ie using
21 donated bone material) are still the main source of
22 material for bone repair, despite the risk of disease
23 transmission, notably HIV or CJD, due to contaminated
24 sources. Both of the current approaches also suffer
25 other disadvantages: the need to obtain bone from the

1 patient for use in the auto-graft requires further
2 invasive procedure(s) and a second wound site in the
3 patient; and the bio-compatible materials currently
4 available are not suitable for all types of bone repair
5 and are particularly inadequate for repairing defects
6 of the skull.

7
8 The present invention provides a biodegradable
9 composite material suitable for implantation in a
10 patient's body, said composite material comprising
11 water-soluble glass and a biodegradable polymer.

12
13 The water-soluble glass material may be in the form of
14 fibres, particles or mixtures thereof. As used herein
15 the term "glass fibres" refers to glass in both wool
16 and mono-filament form. The length of the fibres is
17 not critical and would normally be chosen to suit the
18 size of composite required.

19
20 Examples of suitable water-soluble glass fibres include
21 the fibres described in WO-A-98/54104, WO-A-99/62834
22 and WO-A-99/62835 (all in the name of Giltech Limited),
23 the content of each of these publications being
24 incorporated herein by reference.

25
26 The biodegradable polymer may be any suitable bio-
27 compatible polymer or mixtures of such polymers.
28 Preferably the polymer exhibits some pliability or
29 plasticity. Examples include (but are not limited to)
30 polyvinyl alcohols, polysaccharides (for example
31 alginates and chitosan), polyglycolic acid, polylactic
32 acid, polyglycolactide, polyhydroxybutyrate,
33 polyhydroxyvalerate, polycaprolactones (for example
34 poly ϵ -caprolactone), polycaprolactam and starches
35 (especially "thermoplastic" starches such as
36 hydroxypropylated starches, or potato, maize or rice

1 starch treated by high pressure and humidity). Co-
2 polymers of these polymers may also be used (for
3 example polyglycolide (or polyglycolic acid)/
4 polycaprolactone co-polymer or a polyglycolic
5 acid/polycaprolactam co-polymer).

6
7 A preferred biodegradable polymer is poly(ϵ -
8 caprolactone), or any other slowly degrading polymer
9 material.

10
11 In one embodiment, the water-soluble glass material
12 will degrade more slowly (and usually at a
13 significantly slower rate) than the biodegradable
14 polymer. Alternatively, the biodegradable polymer will
15 degrade more slowly than the water-soluble glass
16 material.

17
18 Advantageously the glass material, in addition to
19 contributing to the strength of the composite material,
20 will provide a suitable environment for initiation of
21 bone repair. Desirably therefore osteoblasts are able
22 to penetrate the biodegradable polymer in order to
23 attach to the glass material and commence bone
24 formation. Generally the size of the glass material
25 will be selected to degrade in a time-scale comparable
26 to bone repair.

27
28 The polymer provides a sponge-like environment around
29 the water-soluble glass, and becomes wetted by body
30 fluids when the composite material is placed in the
31 body. Where water-soluble glass particles or fibres
32 are present in the composite, slight dissolution of
33 polymer occurs around the sites where the glass is
34 present and may cause a general loosening of the
35 composite. The degree of loosening may be beneficial
36 in some embodiments since the areas created are

1 available for tissue ingrowth. Loss of mechanical
2 strength in the composite material may be countered by
3 including randomly orientated fibres and/or the release
4 of zinc ions from the glass, which would promote cross-
5 linking and repolymerisation of the polymer (especially
6 poly ϵ -caprolactone) around the glass.

7
8 A further advantage of the composite described is that
9 it is mouldable, and it may be contoured to fit the
10 implant site closely.

11
12 The composite material may comprise a matrix of water-
13 soluble glass material, the matrix being impregnated
14 with the biodegradable polymer. Optionally the glass
15 material (fibres and/or particles) is arranged to
16 provide adequate strength in the load-bearing
17 dimensions of the composite.

18
19 In a further aspect the present invention provides a
20 method of repairing an area of defective tissue (for
21 example nerve or bone) in a patient, said method
22 comprising implanting a composite material as described
23 above into said patient in sufficient quantity to cover
24 and/or fill said area. Optionally said composite
25 material is attached to healthy tissue using
26 conventional (preferably biodegradable) means. Mention
27 may be of sutures and biodegradable glue in this
28 respect.

29
30 The biodegradable composite of the present invention
31 may be used to form pins, plates, nuts or bolts to hold
32 shattered bone pieces together, or may be formed into
33 flexible sheet form to wrap around a defective tissue.

34
35 In a further aspect, the present invention provides a
36 method of producing a composite material suitable for

1 tissue repair, said method comprising:

2

3 a) providing water-soluble glass fibres and/or
4 glass particles;

5 b) optionally arranging said fibres and/or
6 particles into a pre-selected order;

7 c) covering said fibres and/or particles with a
8 biodegradable polymer and if required allowing
9 said polymer to cure.

10

11 In one embodiment the composite material may be formed
12 using liquid moulding techniques. For example the
13 required array of glass fibres and/or particles may be
14 positioned in a closed mould cavity into which the
15 polymer is then introduced. A rigid composite material
16 is formed once the polymer has cured. Optionally
17 introduction of the polymer into the mould may be
18 vacuum assisted.

19

20 Where poly(ϵ -caprolactone) is used as the polymer,
21 conducting the polymerisation reaction within the mould
22 cavity itself may be desirable since introduction of
23 this polymer into the mould is difficult due to the
24 high viscosity of poly(ϵ -caprolactone). A ring-opening
25 polymerisation of caprolactone using 1,4-butanediol
26 catalyzed with diethylzinc may be suitable for such in
27 situ polymerisation.

28

29 Alternatively, a suitable composite material may be
30 produced by forming glass fibre into a glass fibre
31 fabric which can then be simply dipped into the plastic
32 polymer. Alternatively, the polymer may be sprayed
33 onto the fibre. In addition to the techniques of
34 thermoforming and weaving, the glass fibres could also
35 be spun into a yarn, the fibres or yarn being
36 optionally knitted, braided or crocheted. Likewise

1 where glass wool is used, the wool may be shaped as
2 required and either dipped into the plastic polymer or
3 placed into a closed mould cavity for liquid moulding
4 as described above.

5
6 In a further embodiment glass particles are used
7 together with short lengths of glass fibres.

8
9 In a yet further aspect, the present invention provides
10 the use of a composite material as described above for
11 repairing damaged or defective tissue (especially bone
12 or nerve tissue) in a body.

13
14 Desirably the composite material is sterilised prior to
15 implantation in the body, for example by irradiation.

16
17 Phosphorous pentoxide (P_2O_5) is preferably used as the
18 glass former.

19
20 Generally the mole percentage of phosphorous pentoxide
21 in the glass composition is less than 85%, preferably
22 less than 60% and especially between 30-60%.

23
24 Alkali metals, alkaline earth metals and lanthanoid
25 oxides or carbonates are preferably used as glass
26 modifiers.

27
28 Generally, the mole percentage of alkali metals,
29 alkaline earth metals and lanthanoid oxides or
30 carbonates is less than 60%, preferably between 40-60%.

31
32 Boron containing compounds (eg B_2O_3) are preferably used
33 as glass additives.

34
35 Generally, the mole percentage of boron containing
36 compounds is less than 15% or less, preferably less

1 than 10%, and usually around 5% or less.

2

3 Other compounds may also be added to the glass to
4 modify its properties, for example SiO_2 , Al_2O_3 , SO_3 or
5 transition metal compounds (eg. first row transition
6 metal compounds). Generally, the glass will release
7 ionic species upon dissolution, the exact ionic species
8 released depending upon the compounds added to the
9 glass. Glasses which release aluminium ions, sulphate
10 ions or fluorine ions may be desirable in some
11 circumstances.

12

13 Typically the soluble glasses used in this invention
14 comprise phosphorus pentoxide (P_2O_5) as the principal
15 glass-former, together with any one or more
16 glass-modifying non-toxic materials such as sodium
17 oxide (Na_2O), potassium oxide (K_2O), magnesium oxide
18 (MgO), zinc oxide (ZnO) and calcium oxide (CaO). The
19 rate at which the glass dissolves in fluids is
20 determined by the glass composition, generally by the
21 ratio of glass-modifier to glass-former and by the
22 relative proportions of the glass-modifiers in the
23 glass. By suitable adjustment of the glass
24 composition, the dissolution rates in water at 38°C
25 ranging from substantially zero to $25\text{mg}/\text{cm}^2/\text{hour}$ or more
26 can be designed. However, the most desirable
27 dissolution rate R of the glass is between 0.01 and
28 $2.0\text{mg}/\text{cm}^2/\text{hour}$.

29

30 The water-soluble glass is preferably a phosphate
31 glass, and may comprise a source of silver ions
32 which may advantageously be introduced during
33 manufacture as silver orthophosphate (Ag_3PO_4). Other
34 metals may alternatively or additionally be present and
35 mention may be made of Cu, Mg, Zn, Ce, Mn, Bi, Se, Cs.
36 Preferred metals include Ag, Cu, Zn and Mg. The glass

1 preferably enables controlled release of metal and
2 other constituents in the glass and the content of
3 these additives can vary in accordance with conditions
4 of use and desired rates of release, the content of
5 metal generally being up to 5 mole %. While we are
6 following convention in describing the composition of
7 the glass in terms of the mole % of oxides, of halides
8 and of sulphate ions, this is not intended to imply
9 that such chemical species are present in the glass nor
10 that they are used for the batch for the preparation of
11 the glass.

12
13 The optimum rate of release of metal ions into an
14 aqueous environment may be selected by circumstances
15 and particularly by the specific function of the
16 released metal. The invention provides a means of
17 delivering metal ions to an aqueous medium at a rate
18 which will maintain a concentration of metal ions in
19 said aqueous medium of not less than 0.01 parts per
20 million and not greater than 10 parts per million. In
21 some cases, the required rate of release may be such
22 that all of the metal added to the system is released
23 in a short period of hours or days and in other
24 applications it may be that the total metal be released
25 slowly at a substantially uniform rate over a period
26 extending to months or even years. In particular cases
27 there may be additional requirements, for example it
28 may be desirable that no residue remains after the
29 source of the metal ions is exhausted or, in other
30 cases, where the metal is made available it will be
31 desirable that any materials, other than the metal
32 itself, which are simultaneously released should be
33 physiologically harmless. In yet other cases, it may
34 be necessary to ensure that the pH of the resulting
35 solution does not fall outside defined limits.
36

1 Generally, the mole percentage of these additives in
2 the glass is less than 25%, preferably less than 10%.

3
4 Embodiments of the invention will be described with
5 reference to the following non-limiting examples.

6
7 **Example 1**

8
9 Method of forming a glass fibre

10
11 The glass-forming composition is initially heated to a
12 melting temperature of 500°-1200°C, preferably 750°-
13 1050°C. The temperature is then slowly lowered to the
14 working temperature at which fibre formation occurs.

15
16 Generally, the working temperature of the glass will be
17 at least 200°C lower than the temperature at which the
18 glass is initially heated. Suitable working
19 temperatures may fall within the following ranges 400°-
20 500°C, 500°-900°C (preferably 550°-700°C, more
21 preferably 550°-650°C, especially 600°-650°C) and 800°-
22 1000°C. The working temperature selected will depend
23 upon the glass composition, but an approximate
24 indication of a suitable working temperature can be
25 established as hereinafter described. Depending upon
26 the glass composition used, the working temperature may
27 be a range of suitable temperatures. The range of
28 working temperatures may be narrow, for example of only
29 10°C, so that fibre formation may occur only between
30 the temperature of N°C to (N+10)°C. Other glass
31 compositions may have a wider temperature range for the
32 working temperature in which glass formation is
33 possible.

34
35 Alternatively, the working temperature of the glass may
36 be defined as 50-300°C above the T_g of the glass.

1 In order to obtain an approximate indication of the
2 working temperature for any particular glass
3 composition, the glass composition should be slowly
4 heated to its melting point. As soon as the glass is
5 molten, frequent attempts to pull the composition
6 upwardly to form a fibre should be made, with the
7 temperature of the composition being very gradually
8 increased between attempts. The temperature range of
9 the composition during which fibre formation is
10 possible should be noted and used as a preliminary
11 working temperature in the process of the invention.
12

13 It will be clear to those skilled in the art that the
14 pulling speed at which the fibre is drawn off can
15 affect the choice of working temperature and the
16 diameter of the fibre required. Where a fibre of
17 relatively large diameter is required, the fibre tends
18 to be pulled more slowly and the working temperature
19 may need to be decreased slightly. Where a fibre of
20 relatively small diameter is required (eg a glass
21 wool), the fibres may be drawn at the much higher
22 pulling speed and the working temperature may need to
23 be increased (thus lowering the viscosity of the
24 composition to accommodate the increased pulling
25 speed). Selection of the exact working temperature in
26 respect of any particular fibre size and composition
27 will be a simple matter of routine evaluation of
28 optimal process conditions.
29

30 With reference to the "working temperature" of the
31 glass, the skilled person will appreciate that the
32 furnace temperature may differ considerably from the
33 temperature of the glass itself and indeed there may be
34 a significant temperature gradient in the glass.
35 Ideally the "working temperature" will be the
36 temperature of the glass as fibre formation (ie.

1 pulling) takes place. In many compositions however, it
2 may not be practical to measure the temperature at the
3 surface of the glass where pulling occurs by insertion
4 of a temperature probe as the introduction of the probe
5 may precipitate crystallisation of the glass. One
6 alternative is to place a temperature probe into the
7 bushing and to monitor the bushing temperature which
8 will be a good indicator of the glass temperature at
9 the moment of fibre formation. Alternatively an Infra
10 Red pyrometer may be focused onto the appropriate area
11 of the glass and used to monitor the temperature.

12
13 The glass to be formed into fibres will generally be
14 heated until molten, optionally clarified, and then
15 cooled slowly and controllably until the appropriate
16 working temperature is reached and fibre formation can
17 commence. The initial heating of the glass above its
18 melting point and the subsequent fibre formation may be
19 carried out in a single vessel or, alternatively, the
20 molten glass may be transferred to a vessel designed
21 specifically for fibre formation. One way of holding
22 the molten glass in a vessel having a bushing within
23 its lower surface until the temperature drops to the
24 required working temperature is to coat or fill the
25 holes of the bushing with a material that gradually
26 melts over the period of time taken for the glass to
27 reach the temperature required.

28
29 The most important aspect of the method is the manner
30 in which the working temperature is reached. We have
31 found that the molten glass, which may preferably be
32 heated significantly above its melting point, should be
33 allowed to cool in a highly controlled manner, the
34 temperature being only gradually reduced until the
35 working temperature is reached. A stirrer may be
36 present to ensure that the temperature of the whole of

1 the molten glass is kept as uniform as possible.

2

3 The glass is cooled to a temperature at which the glass
4 will not crystallise for at least the period of time
5 needed to convert the melt to fibre. This temperature
6 is termed herein as a "holding temperature". The rate
7 of cooling from this holding temperature is determined
8 by the rate at which the melt is consumed at the
9 bushing and the difference in temperature between the
10 bushing temperature (the working temperature) and the
11 melt holding temperature.

12

13 Due to low viscosity and narrow temperature band for
14 many of these compositions, control of the balance
15 between melt temperature, bushing temperature and glass
16 throughput rate is critical.

17

18 Examples 2 to 16 detail suitable compositions which can
19 be formed into fibres using the method of Example 1.
20 Alternatively, these glasses can be cast in a
21 conventional way and used to form particles, powder or
22 granules.

23

24 Example 2

25	Component	Mole %
26 Glass Composition		
27	Na ₂ O	31.05
28	CaO	16.00
29	Ag ₂ O	3.88
30	P ₂ O ₅	46.08
31	Na ₂ PO ₃ F	0.97
32	2Al ₂ O ₃ .B ₂ O ₃	2.00

33

34 100 grams of the sample was heated to 900°C before
35 being cooled and pulled at 650°C, at 25 km/hr. Overall
36 the fibre was good; one sample was 10 km in length and

1 11 grams in weight, although there was some
2 crystallisation at the pulling temperature.

3

4 **Example 3**

5	Component	Mole %
6 Glass Composition		
7	Na ₂ O	29.51
8	CaO	15.21
9	Ag ₂ O	3.68
10	P ₂ O ₅	43.80
11	2Al ₂ O ₃ .B ₂ O ₃	1.90
12	Na ₂ PO ₃ F	1.90
13	Na ₂ B ₄ O ₇ .10H ₂ O	1.00
14	Na ₂ PO ₄	3.00

15

16 74 grams of the sample was heated to 1000°C before
17 being cooled and pulled at 635°C at 25 km/hr. The
18 fibre produced was ultrafine; one sample was 18 km in
19 length and 59 grams in weight. The sample was sprayed
20 with WD40 to prevent water absorption and to aid
21 lubricity. There was some debris at the bottom of the
22 crucible, but this was found to be just iron deposits
23 from the brushing rod.

24

25 **Example 4**

26	Component	Mole %
27 Glass Composition		
28	Na ₂ O	34.20
29	CaO	16.15
30	P ₂ O ₅	44.65
31	Na ₂ SO ₄	5.00

32

33 200 grams of the sample was heated to 1050°C before
34 being cooled and pulled at 635°C at 25 km/hr. The
35 fibre was good although there was some crystallisation
36 at the pulling temperature.

1 **Example 5**

2		Component	Mole %
3	Glass Composition		
4		Na ₂ O	32.40
5		CaO	15.30
6		P ₂ O ₅	42.30
7		2Al ₂ O ₃ .B ₂ O ₃	3.00
8		Na ₂ PO ₃ F	1.00
9		Na ₂ SO ₄	6.00

10

11 117 grams of the sample was heated to 950°C before
12 being cooled and pulled at 635°C, at 40 km/hr. The
13 fibre produced was good and there were no
14 crystallisation problems even though the surface
15 temperature of the fibre dropped to 510°C in the
16 pulling process.

17

18 **Example 6**

19		Component	Mole %
20	Glass Composition		
21		Na ₂ O	31.71
22		CaO	14.73
23		P ₂ O ₅	36.33
24		B ₂ O ₃	4.78
25		SO ₃	9.40
26		Na ₂ PO ₃ F	3.00

27

28 99 grams of the sample was heated to 800°C before being
29 cooled to 650°C and pulled at 40 km/hr. The fibre
30 produced was very fine but difficult to pull and quite
31 fragile at speed.

32

33

34

35

36

1 **Example 7**

2	Component	Mole %
3 Glass Composition		
4	Na ₂ O	30.77
5	CaO	14.28
6	P ₂ O ₅	35.28
7	B ₂ O ₃	4.64
8	SO ₃	9.12
9	FePO ₄	2.41
10	Na ₂ PO ₃ F	0.20
11	Na ₂ PO ₃ F	0.20
12	MnHPO ₄	2.06

13
14 200 grams of the sample was heated to 850°C before
15 being cooled to 545°C and pulled at 40 km/hr. The
16 fibre produced was strong and thin; there was not a
17 problem of crystallisation, in fact the glass can be
18 stored at 550°C for 72 hours without the onset of
19 crystallisation.

20

21 **Example 8**

22 Below is an example of a wool formulation and running
23 conditions to illustrate the differences with the
24 monofilament examples given above.

25

26 A typical wool formulation is

27

28	Na ₂ O	26.31
29	CaO	17.78
30	P ₂ O ₅	47.04
31	B ₂ O ₃	5.94
32	MnO	1.55
33	Fe ₂ O ₃	0.97
34	NaF	0.41

35

36 Solution rate, non annealed = 0.0278 mg.cm⁻²hr⁻¹

37 Melted and refined at 1000°C.

38 Cooled and held at 725°C.

39 Bushing temperature maintained at 365°C.

1 Thick fibres approx 1.2mm diameter drawn through pinch
2 rollers at 2.5 M.mm^{-1} from a bushing with 6 x 6.5mm
3 diameter holes. Fibres jet attenuated to produce a
4 fine wool 5 -15 μm diameter. The wool was sprayed with
5 silicone oil finish during the attenuation process and
6 collected on a stainless steel mesh conveyor.
7 Typically, attenuated wools will have diameters of 5 to
8 20 μm . Monofilament fibres will mostly be 20 to 50 μm
9 diameter.

10

11 **Example 9**

12	Na_2O	31.19 mole %
13	K_2O	9.63 mole %
14	Ag_2O	2.9 mole %
15	B_2O_3	2.74 mole %
16	2NaF	0.66 mole %
17	P_2O_5	52.88 mole %

18 Furnace at 710°C - 800°C.

19 Bushing at 450°C - 460°C.

20 4.5mm bushing holes.

21 50km per hour pull rate.

22 Good fibres.

23 Solution rate = 1.68 not annealed 2.28 annealed.

24

25 **Example 10**

26	Na_2O	32 mole %
27	K_2O	10 mole %
28	Ag_2O	3 mole %
29	P_2O_5	55 mole %

30

31 Furnace at 850°C.

32 Bushing at 530°C.

33 5mm bushing holes.

34 55kmph.

35 Good strong fibres.

36

37

38

39

1 **Example 11**

2 Na₂O 32 mole %
3 K₂O 10 mole %
4 (MgO 4 mole %) - added as an anti-microbial
5 B₂O₃ 5 mole %
6 Ag₂O 3 mole %
7 P₂O₅ 46 mole %

8
9 Furnace temperature 650°C - 730°C.
10 Bushing temperature 410°C - 420°C.
11 Bushing 5.5mm diameter.
12 Speed up to 100kmph.
13 Solution rate 0.7 annealed 1.0 non annealed (mg.cm⁻³.hr⁻¹).
14 Very good strong reliable fibre. Very stable.

15

16 **Example 12**

17 Na₂O 36.68 mole %
18 K₂O 8.63 mole %
19 P₂O₅ 45.09 mole %
20 B₂O₃ 5.29 mole %
21 Ag₂O 2.59 mole %
22 (CaO 1.73 mole % to attenuate solution rate!

23

24 Furnace temperature 550°C.
25 Bushing 62 x 5.0mm holes.
26 Bushing temperature 400°C.
27 Speed 80kmph.
28 Very good fibres.
29 Solution rate 3.11 annealed, 3.8 non annealed (mg.cm⁻².hr⁻¹).

30

31 The fibres show excellent tensile strength, flexibility
32 and shock resistance.

33

34 The fibres are especially suitable for industrial and
35 plastics reinforcement controlled release (anti-
36 microbial, anti-corrosion etc) and rapidly
37 biodegradable applications.

38

39

Example 13

CaO 30 mole %
MgO 20 mole %
P₂O₅ 50 mole %

5

6 Furnace at 1050°C.

7 Bushing 5.5mm holes.

8 Bushing temperature 700°C - 720°C.

9 Speed up to 80kmph.

10 Solution rate TBA.

11 Very strong fibre.

12

Example 14

(K₂O 5 mole %) Trace to alter dissolution rate
CaO 25 mole %
Mg₂O 20 mole %
P₂O₅ 50 mole %

18

19 Furnace 1000°C.

20 Bushing 5.5mm.

21 Bushing temperature 560°C - 620°C.

22 Speed up to 70kmph.

23 Solution rate TBA.

24 Very strong fibre.

25 Anti-microbial.

26

Example 15

CaO 28.5 mole %
MgO 18.5 mole %
Ag₂O 3 mole %
P₂O₅ 50 mole %

32

33 Furnace temperature 1050°C - 1150°C.

34 Bushing 4 x 5.5mm.

35 Bushing temperature 700°C.

36 Speed 50kmph.

37 Solution rate TBA.

38 Very good, strong fibre.

39 Anti-microbial.

1 **Example 16**

2 CaO 30 mole %
3 MgO 20 mole %
4 P₂O₅ 50 mole %

5

6 As Example 15 (without silver)

7

8 The fibres show excellent tensile strength, flexibility
9 and shock resistance. These fibres are suitable for
10 applications requiring slower release and greater
11 tensile strength plus biodegradability. The fibres are
12 suitable for orthopaedic implants and tissue
13 engineering applications.

14

15 **Example 17**

16 Producing a composite comprising soluble glass powder
17 or granules.

18

19 Glass powder or granules can be added to the polymer to
20 reinforce, stiffen or bulk the composite. The glass
21 (for example based on the glasses of any of Examples 1
22 to 16) can be used to release, for example,
23 antimicrobials or trace elements. The glass, whose
24 solution rate can be varied as required, reduces the
25 volume of polymer to be degraded when used as a bulking
26 agent.

27

28 The powder or granules/polymer composition can be made
29 in various ways, as follows:

30

31 1. Mixing the glass with solvent dissolved polymer,
32 e.g. polycaprolactone can be dissolved in
33 chloroform. Glass is added to the liquid and
34 mixed. The solvent is evaporated to leave the
35 composite.

36

37 2. The glass can be mixed into melted polymer.

38

39 3. The glass can be added to polymer masterbatch

1 which can then be used in extrusion or co-
2 extrusion processes.

3

4 **Example 18**

5 Producing a composite comprising soluble glass fibre.

6

7 The addition of biodegradable glass fibre (as described
8 in any of Examples 1 to 16) for reinforcement, bulking
9 or controlled release in the polymer may be achieved by
10 various methods, as follows:

11

12 1. Fibre can be passed through a bath of polymer
13 dissolved in solvent. The polymer solution can
14 also be applied by passing the fibre over a
15 rotating or counter-rotating transfer roller.

16

17 2. Solvent dissolved polymer can be sprayed directly
18 onto fibre as it is collected onto a drum or
19 atomised into the jet attenuation venturi to
20 produce coated wool.

21

22 3. Continuous fibre can be fed through a bath of
23 melted polymer.

24

25 4. Fibre can be mixed into melted polymer or knitted
26 or pre-formed into shapes to be layered into
27 melted polymer. It may be possible to make sheets
28 of polymer/fibre "sandwich" which can be thermally
29 formed in a press.

1 CLAIMS

2

3 1. A biodegradable composite material suitable for
4 implantation into a patient's body, said composite
5 material comprising water-soluble glass and a
6 biodegradable polymer.

7

8 2. The composite material as claimed in Claim 1,
9 wherein said biodegradable polymer is a polyvinyl
10 alcohol, polysaccharide, polyglycolic acid,
11 polylactic acid, polyhydroxybutyrate,
12 polyhydroxyvalerate, polycaprolactone,
13 polycaprolactam or a starch.

14

15 3. The composite material as claimed in Claim 2
16 wherein said biodegradable polymer is poly ϵ -
17 caprolactone.

18

19 4. The composite material as claimed in any one of
20 Claims 1 to 3 wherein said water-soluble glass is
21 in the form of glass fibres and/or particles.

22

23 5. The composite material as claimed in any one of
24 Claims 1 to 4 which comprises a matrix of water-
25 soluble glass fibres and/or particles impregnated
26 with said biodegradable polymer.

27

28 6. A method of repairing an area of defective tissue
29 in a patient, said method comprising inserting the
30 composite material as claimed in any one of Claims
31 1 to 5 into said patient in a quantity sufficient
32 to cover and/or fill said area.

33

34 7. The method as claimed in Claim 6 wherein said
35 tissue is nerve or bone.

36

37 8. The method as claimed in either one of Claims 6
38 and 7 wherein said composite material is attached
39 to healthy tissue by suture and/or by

1 biodegradable adhesive.

2

3 9. A method of producing a composite material
4 suitable for tissue repair, said method
5 comprising:

6

7 a) providing water-soluble glass fibres and/or
8 glass particles;

9 b) optionally arranging said fibres and/or

10 particles into a pre-selected order;

11 c) covering said fibres and/or particles with a
12 biodegradable polymer and if required allowing
13 said polymer to cure.

14

15 10. The method as claimed in Claim 9 wherein said
16 biodegradable polymer is poly ϵ -caprolactone and
17 wherein polymerisation occurs within the mould.

18

INTERNATIONAL SEARCH REPORT

Internat'l Application No

PCT/GB 00/00475

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61L27/58 A61L27/42 A61L27/46 A61L31/14 A61L31/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X	DATABASE WPI Section Ch, Week 199904 Derwent Publications Ltd., London, GB; Class A14, AN 1999-040635 XP002138589 & JP 10 298108 A (DAINIPPON INK & CHEM INC), 10 November 1998 (1998-11-10) abstract -/-	1,2,6-8



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
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X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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INTERNATIONAL SEARCH REPORT

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